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13. ABSTRACT ***(Maximum 200 Words)***

Ovarian carcinoma cells from patient were fused to autologous and allogeneic dendritic cells (DC). The fusion cells co-expressed tumor-associated antigens derived from ovarian carcinoma cells and DC-derived co-stimulatory molecules. Fusion cells retained the functional potency of DC and stimulated autologous T cell proliferation in vitro. These T cells derived from patients with metastatic ovarian cancer induced MHC class I-restricted lysis of autologous ovarian tumor cells, but not monocytes, allogeneic ovarian carcinoma cells or MUC1 positive tumor cell lines. These findings indicate that fusions of human ovarian cancer cells with autologous or allogeneic DC induce specific antitumor immune response against autologous ovarian cancer cells.

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INTRODUCTION:

Dendritic cells (DC) have been fused to carcinoma cells. The hybrid cells express DC-derived MHC class I and II and costimulatory molecules as well as tumor-derived antigens. Immunization with fusion cells elicit specific and potent antitumor immunity and eradicate established pulmonary metastasis in animal model. We propose to extend these findings to humans using ovarian carcinoma as tumor model. Human ovarian carcinoma cells express the CA-125, HER2/neu and MUC1 tumor-associated antigens as potential targets for the induction of active specific immunotherapy. We successfully fused human ovarian carcinoma cells with autologous (auto) or allogeneic (allo) DC. Both auto- or allo-fusion cells induced cytolytic activity and lysis of autologous tumor cells.

BODY:

In the first year of funding, my human protocol and consent form have approved by Dana-Farber cancer institute IRB previously need to be revised according to the requirements of the U.S. Army regarding to human subjects protection. In the April 30, 2001, the revised human protocol and consent form have been approved by both DFCI IRB and U.S. Army Medical Research and Materiel Command, human subjects protection specialist, Dr Howard (see attachment). We are waiting for the final approval by the Army and reinitiate the study. Even so, we obtained very interesting results based on the previous studies. Ovarian cancer cells from patients have been successfully fused to autologous and allogeneic DC. Both auto- and allo-DC/tumor fusion cells express the CA-125 and MUC1 antigens, MHC class II, B7-1 and B7-2. Autologous T cells cocultured with auto- or allo-DC/tumor fusion cells resulted in the proliferation. Moreover, both fusion cells induced cytolytic T cell activity and lysis of autologous tumor cells by a MHC class I-restricted mechanism.

DISCUSSION:

We have developed a vaccine based on the fusions of DC with ovarian cancer cells. The fusion cells express MHC class I and II, costimulatory molecules and tumor-derived peptides. They are well equipped to activate T cells in the right environment. We demonstrate that auto- or allo-DC/ovarian cancer fusion cells are potent stimulators of autologous T cells. Both fusion cells induce specific CTL activity and lysis of autologous tumor cells.

In the coming year, we will study on more case of patients for the effective of fusion cell, and also will focus on the fusion cells of ovarian carcinoma cells with HLA-matched or unmatched allogeneic DC. Both fusion cells will be assessed

phynotypically and functionally. We will also study the basis of CTL generation and analyze the CTL stimulated by autologous fusion cells.

CONCLUSIONS:

- Ovarian cancer cells can be fused to either allogeneic or autologous DC.
- Fusion cells express MHC class I and class II, co-stimulatory molecules, ICAM and tumor antigens.
- Both allogeneic and autologous DC fused with patients-derived OVCA can efficiently stimulate the patient's T cell proliferation.
- CTL generated by fusion cells demonstrate strong lysis of autologous OVCA cells.

PUBLICATIONS

1. Gong J., Nikrui N., Chen D., Koido S., Wu Z., Tanaka Y., Cannistra S., Avigan D. and Kufe D. Fusion of Human Ovarian Carcinoma Cell with Autologous and Allogenic Dendritic cells Induce Anti-Tumor Immunity. J. Immunol. 2000, 165:1705-1711.